IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION		DOCKET NO.:	47679
OF:	VON DEYN ET AL.	CONFIRM. NO.:	4798
SERIAL NO.:	09/091,300	GROUP ART UNIT:	1626
FILED:	JUNE 16, 1998	EXAMINER:	R. H. HAVLIN

FOR: 3-HETEROCYCLYL-SUBSTITUTED BENZOYL DERIVATIVES

Honorable Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. §1.132

Sir:

I, Matthias Christian Witschel, a doctor of natural sciences, a citizen of the Federal Republic of Germany and residing at Höhenweg 12B, 67098 Bad Dürkheim, Germany, declare as follows:

I am a fully trained chemist, having studied chemistry at the University of Erlangen-Nuremberg, Germany, from 1985 to 1994;

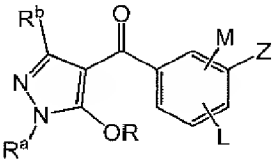
I was awarded my doctor's degree by the University of Erlangen-Nuremberg in 1994; I was a post-doctoral fellow at the Stanford University from 1994 to 1995;

I joined BASF SE, formerly named BASF Aktiengesellschaft of 67056 Ludwigshafen, Germany, in 1996, and since then I have been engaged in the synthesis of herbicides and herbicide screening, and I am therefore fully conversant with the technical field to which the invention disclosed and claimed in application Serial No. 09/091,300 belongs;

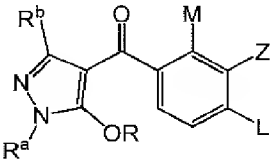
I am the Matthias Witschel who is named as one of the inventors of the invention disclosed and claimed in Application No. 09/091,300, and the Matthias Christian Witschel who executed the Declarations previously filed in this application on October 21, 1999, and signed by me on October 21, 1999; therefore, I am familiar with the prosecution history of the application and with the prior art cited therein.

I have studied the Office actions which issued in this case on November 24, 2010, and on August 01, 2011, and the references cited therein, in particular the teaching of ***von Deyn et al.*** as provided in ***WO 96/26206*** and the U.S. counterpart thereof, ***US 5,846,907***, as well as the disclosure of ***Silverman*** regarding "*Drug Discovery, Design, and Development*" in Chapter 2 of "The Organic Chemistry of Drug Design and Drug Action," Academic Press, Inc. San Diego 1992, pp. 4-51. It is my understanding that the Office actions assert that the structural particularities of the 3-heterocyclyl-substituted benzoyl compounds of formula (I) as disclosed and claimed in application Serial No. 09/091,300, as well as the activity and effectivity of the compounds, were already well within the purview of a person working in the field of herbicidal ingredients in view of the teaching of ***von Deyn et al.*** and the disclosure of ***Silverman*** essentially because

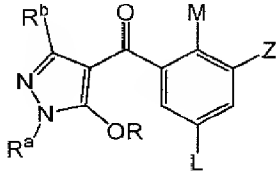
- ***von Deyn et al.*** teach herbicidal pyrazolylbenzoyl compounds represented by formula (i), including embodiments represented by formulae (ia) and (ib),



(i)



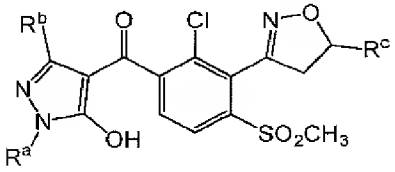
(ia)



(ib)

which are generic to the compounds of formula (I) of the present application;

- ***von Deyn et al.*** *inter alia* refer to compounds (i) in which L and M are hydrogen, methyl, methoxy, methylthio, chlorine, cyano, methylsulfonyl, nitro, or trifluoromethyl;
- ***von Deyn et al.*** *inter alia* describe the pyrazolylbenzoyl compounds:



No.	R^a	R^b	R^c
1.79*	CH_3	CH_3	CN
5.4	CH_3	CH_3	H
5.5	CH_2CH_3	H	H

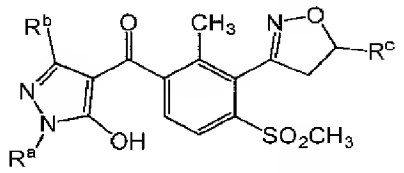
* designation as used in US 5,846,907, the respective compound is designated as No. 1.267 in the corresponding WO 96/26206

and

- ***Silverman*** *inter alia* describes Cl and CH_3 as classical isosteres and, allegedly, that substituting one for the other would yield compounds having the same utility.

However, although the compounds of ***von Deyn et al.*** and those disclosed and claimed in application Ser. No. 09/091,300 have the same utility, it is my opinion that the data provided

in my previous Declaration of October 21, 1999 (declaration having 4 pages; in the following also referred to as "Declaration 1"), show that the compounds of application Ser. No. 09/091,300 distinctly differ from the compounds of ***von Deyn et al.*** in their effectivity. Tables 2, 3 and 4 of Declaration 1 show the results of investigations into the efficacy of the three aforementioned 4,5-dihydroisoxazolyl substituted compounds of ***von Deyn et al.*** in comparison with compounds which differed structurally solely in that the 1-chlorine substituent was replaced by a methyl group, i.e.,



No.	R^a	R^b	R^c
B	CH_3	CH_3	CN
A	CH_3	CH_3	H
3.90	CH_2CH_3	H	H

For convenience, the respective data are reproduced in the following Tables 1A to 1C:

Table 1A (*the data and results are set forth in Table 4 on page 4 of Declaration 1*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of prior art compound 1.79 and comparative compound **B**:

Application Rate	250 g/ha		125 g/ha	
Compound	**B**	1.79	**B**	1.79
Amaranthus retroflexux	**90**	40	**90**	30
Echinochloa crus-galli	**90**	70	**85**	40
Chenopodium album	**98**	90	**95**	90
Setaria viridis	**70**	40	**50**	30

Table 1B (*the data and results are set forth in Table 3 on page 3 of Declaration 1*) Comparison of the efficacy (*plant damage in percent*) of prior art compound 5.4 and comparative compound **A** as disclosed and claimed in application Ser. No. 09/091,300:

Application Rate	62.5 g/ha		31.2 g/ha	
Compound	**A**	5.4	**A**	5.4
Abutilon theoprasti	**90**	85	**85**	65
Brachiaria platyphylla	**90**	80	**80**	65
Polygonum persicaria	**98**	75	**70**	65
Sinapis alba	**100**	90	**100**	85
Stellaria media	**100**	90	**100**	85

Table 1C (*the data and results are set forth in Table 2 on page 3 of Declaration 1*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of prior art compound 5.5 and comparative compound **3.90** as disclosed and claimed in application Ser. No. 09/091,300:

Application Rate	62.5 g/ha		31.2 g/ha	
Compound	**3.90**	5.5	**3.90**	5.5
Crop Plant: Zea mays	**10**	20	**0**	0
Unwanted Plants: Abutilon theoprasti	**80**	75	**80**	60
Amaranthus retroflexus	**80**	70	**80**	60
Digitaria sanguinalis	**100**	100	**100**	98
Setaria italica	**95**	90	**90**	85

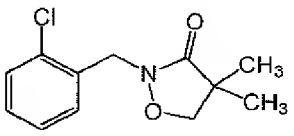
The data compiled in each of the three tables show that the chlorine-substituted prior art compound was, in all instances, less effective against the unwanted plants than the corresponding methyl-substituted compound. In fact, the effectivity of the chlorine-substituted prior art compound against the unwanted plants when used at the higher application rate was, in all but one test, equal or even below that of the corresponding methyl-substituted compound according to the present application when applies at half the application rate.

This finding in and of itself is surprising when the teaching of ***von Deyn et al.*** and the disclosure of ***Silverman*** are considered. The teaching of ***von Deyn et al.*** at best merely conveys that the replacement of one of the radicals in the position designated as "L" in prior art formula (i) for another radical within the definition of "L" is of little consequence. I find nothing in the disclosure of ***Silverman*** which reasonably adds to the teaching of ***von Deyn et al.***

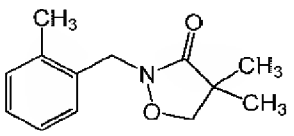
Silverman states that the structural modification of a lead compound along the lines of bioisosterism "*has been shown to be useful to attenuate toxicity or to modify the activity of a lead, and it may have a significant role in the alteration of metabolism of a lead[,]*" and lists a variety of uni-, bi-, tri-, and tetravalent atoms and groups, as well as ring equivalents as examples for classical bioisosteres. Notably, ***Silverman*** explains in the first paragraph on

page 8, that the expression "activity" is used in the reference for "*the particular biological or pharmacological effect (e.g., antibacterial activity or anticonvulsant activity) ... [whereas]* potency *is the strength of that effect*" (*emphasis original*). Thus, ***Silverman***'s remarks regarding bioisosteric replacement indicate that any such modification may alter the nature of the biological or pharmaceutical property of the compound, or may change the compound's toxicity. In my opinion, the statements of ***Silverman*** regarding bioisosterism are by far too general to suggest that any one of the various possible bioisosteric replacements can reasonably be associated with a specific impact on a compound's activity or on its potency as those expressions are used by ***Silverman***. More specifically, I consider the statements of ***Silverman*** to be too general to suggest that any one of the various possible bioisosteric replacements has a specific, or a reasonably predictable, impact on the properties of the particular compounds which are taught by ***von Deyn et al.*** To the contrary, ***Silverman*** further corroborates that the result of a bioisosteric replacement, or any one of the other approaches which are addressed in the chapter "Drug Discovery, Design, and Development," remains unpredictable when concluding the chapter by pointing out: "*On the basis of what was discussed in this chapter, is appears that even if one uncovers a lead it may be a fairly random process to optimize its potency. In fact, less than 1 in 10,000 compounds synthesized in drug companies makes it to the drug market ... .*" Additionally, I find nothing in the disclosure of ***Silverman***, or in the teaching of ***von Deyn et al.***, which would reasonably indicate that among the near 200 compounds which are specifically mentioned by ***von Deyn et al.***, the three examples which carry a 4,5-dihydroisoxazol-3-yl ring in the position of Z of prior art formula (i) are particularly suited as lead compounds.

Also, consonant with the teaching of ***Silverman*** that a structural modification of a lead compound along the lines of bioisosterism may affect the toxicity or the biological effect of a compound, there are many examples in the art which illustrate that replacing a chlorine group in a molecule by a methyl group actually may dramatically reduce the potency of the compound. An illustrative example in the herbicidal art is provided by Examples 16 and 19 of US 4,405,357 and their herbicidal effect:



Example 16



Example 19

The data compiled in Table 1 of US 4,405,357, at cols. 31-32, and cols. 33-34, show that the replacement of the ortho chlorine group of Example 16 by an ortho methyl group, as in Example 19, resulted in an almost complete loss of the herbicidal activity. Enclosed herewith is a marked up copy of US 4,405,357 in which the pertinent sections in columns 11, 12 and 31-34 are highlighted. This further corroborates that the results in application Ser. No. 09/091,300 were surprising indeed.

In addition to the surprising finding that replacing the 1-chlorine substituent of the 4,5-dihydroisoxazol-3-yl-substituted prior art compounds by a methyl group distinctly increased the potency of the herbicidal action against unwanted plants, the data in the foregoing Table 1C show that the replacement also caused the modified compound to be better tolerated by the crop plant than the corresponding chlorine substituted prior art compound. Surprisingly, the methyl-substituted compound in accordance with application Ser. No. 09/091,300 is *less phytotoxic* in its action on Zea mays while, at the same time, being *more phytotoxic* in its action against the unwanted plants. The divergence of the phytotoxic effect of the 1-chlorine substituted prior art compounds and the methyl-substituted counterpart is especially apparent from the data in cols. 3 and 4 of Table 1C. Col. 3 of Table 1C provides the percentage of plant damage caused when prior art compound 5.5 was applied at a rate of *62.5 g/ha*. Col. 4 of Table 1C provides the percentage of plant damage which resulted when half as much of the corresponding methyl-substituted compound **3.90** was applied, i.e., *31.2 g/ha*. Even at the reduced application rate, the methyl-substituted compound **3.90** was more effective against the unwanted plants than the chlorine substituted prior art compound 5.5 was at the higher application rate. Moreover, the methyl-substituted compound **3.90** did not cause harm to the crop plant whereas the chlorine substituted prior art compound 5.5 resulted in 20% damage to the crop plant at the respective application rate. Thus, less of the methyl-substituted compound **3.90** provide better control of the unwanted plants while being less damaging to the crop plant than is the case for the chlorine substituted prior art compound 5.5.

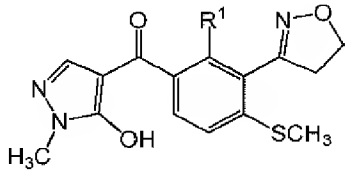
I noticed that little weight has been given in the Office action of August 01, 2011, to the data in Table 4 of my Declaration 1 (*corresponding to Table 1A above*) because the methyl-substituted counterpart of ***von Deyn et al.***'s compound 1.79 is not within the claims currently pending in application Ser. No. 09/091,300. In my opinion, these data nonetheless are relevant because they further corroborate that replacing the chlorine group of the prior art compound 1.79 by a methyl group distinctly increases the herbicidal properties of the

compound. This result is consonant with the results obtained in the investigations addressed in the foregoing Tables 1B and 1C and, therefore, further corroborates that the surprising increase in the herbicidal effectivity which results from the pertinent structural modification is not limited to a specific compound but may reasonably be extrapolated to other compounds within formula (I) in which the groups represented by R^2-R^5, Y and/or R^{15} differ from the specific moieties present in compounds **3.90** and **A.2**.

I also noticed that little weight has been given in the Office action of August 01, 2011, to the investigations and results which are reported in my second Declaration of October 21, 1999 (declaration having 11 pages, in the following also referred to as "Declaration 2") because the respective investigations did not include either one of the prior art compounds 1.79, 5.4, and 5.5, and because the application rates used in the supplemental investigations reported in Declaration 2 were deemed to differ substantially from those of the prior art compounds.

It should be appreciated, however, that the compounds which were addressed in my second Declaration, structurally differ from the chlorine substituted prior art compounds in two or more structural aspects. A comparison of the chlorine substituted prior art compounds with any one of the compounds investigated in the tests reported in Declaration 2, therefore, is unsuited to show the impact on the potency of the compounds which results from the pertinent structural modification. Nonetheless, those data and results can be taken together with the results and comparisons reported in Declaration 1, and the data further corroborate the compounds disclosed and claimed in application Serial No. 09/091,300 exhibit particular unexpected and advantageous properties.

For example, Tables 1 and 5 of Declaration 2 include the results of investigations into the activity of compounds designated as "**A**" (*in the following referred to as "**A.2**" to avoid confusion with compound A of Declaration 1*) and "**E**" against Chenopodium album, Echinochloa crus-galli, and Setaria viridis at an application rate of 250 g/ha, i.e., unwanted plants and application rates similar to those employed in the tests compiled in the foregoing Table 1A.



No.	R^1
A.2	CH_3
E	OCH_3

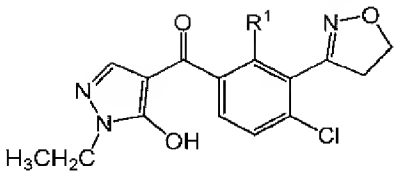
For convenience, the respective data are compiled in the following Table 1D.

Table 1D (*the data are set forth in Tables 1 and 5, on pages 2 and 4, of Declaration 2*) Comparison of the efficacy (*plant damage in percent*) of compounds **A.2** and **E** in accordance with application Ser. No. 09/091,300

Compound	**A.2**	**E**
Chenopodium album	100	95
Echinochloa crus-galli	90	90
Setaria viridis	98	95

It can be seen from these data that, at an application rate of 250 h/ha, the compounds **A.2** and **E** differed by 5% in their effectivity against Chenopodium album, were equally effective against Echinochloa crus-galli, and differed by 3% in their effectivity against Setaria viridis. Replacing a methyl group in the position of R^1 by a methoxy group, accordingly has an impact on the potency of at most 5% at this application rate and against these unwanted plants. Conversely, the data in Table 1A showed that the exchange of methyl and chlorine in the same location of the molecule altered the effectivity against Chenopodium album by 8%, the effectivity against Echinochloa crus-galli by 20%, and the effectivity against Setaria viridis by 30%. Since the compounds **A.2** and **E** on the one hand, and the compounds **B** and 1.79, on the other hand, differ from one another in more than one structural aspect, a comparison of the potencies of these pairs of compounds does not allow a conclusion. However, the trends in the potencies within each pair of compounds can be compared. The data in Tables 1 and 5 of Declaration 2, taken together with those in Table 4 of Declaration 1, thus, show that the variation of the group R^1 within the realm of formula (I) as defined in current Claim 28 has a considerably lower impact on the potency of the compound than the exchange in the position of R^1 for a chlorine radical as is found in the prior art compounds.

Similarly, Tables 14 and 17 of Declaration 2 include the results of investigations into the activity of compounds designated as "**N**" and "**Q**" against Chenopodium album at an application rate of 250 g/ha, i.e., one of the unwanted plants and the application rate employed in tests compiled in the foregoing Table 1A.



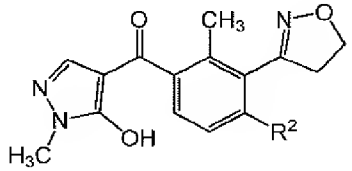
No.	R^1
N	CH_3
Q	SO_2CH_3

Both compounds caused 100% damage to the unwanted plants, i.e., the compounds were equally effective. Conversely, the data in Table 1A showed that the exchange of methyl and chlorine in the same location of the molecule altered the effectivity against Chenopodium album from 98% control for the methyl-substituted compound **B** to 90% of the corresponding prior art compound 1.79 which carries a chlorine group in the position of R^1. Again, the compounds **N** and **Q** on the one hand, and the compounds **B** and 1.79, on the other hand, differ from one another in more than one structural aspect. Thus, no conclusion can be drawn when comparing the potencies of these pairs of compounds. However, the trends in the potencies within each pair of compounds can be compared. The data in Tables 14 and 17 of Declaration 2, taken together with those in Table 4 of Declaration 1, thus, further corroborate that the variation of the group R^1 within the realm of formula (I) as defined in current Claim 28 has a considerably lower impact on the potency of the compound than the exchange in the position of R^1 for the chlorine radical as is found in that position in the prior art compounds.

Further, the data in Tables 2 and 8-11 of Declaration 2 *inter alia* show the effectivity of the compounds designated as **B** (*in the following referred to as "**B.2**" to avoid confusion with compound **B** of Declaration 1*), **H**, **I**, **J**, and **K** at an application rate of 62.5 g/ha against Polygonum persicaria. Accordingly, treatment of the unwanted plant with the respective amounts of the compounds caused 98-100% damage to the plant. Correspondingly, Table 1B illustrates that compound **A** in accordance with application Serial No. 09/091,300 when applied at an application rate of 62.5 g/ha caused 98% damage to Polygonum persicaria, whereas the same amount of the corresponding chloro-substituted prior art compound 5.4 only resulted in 75% damage.

Similarly, the data in Tables 9 and 10 of Declaration 2 *inter alia* show that treatment of Sinapis alba with 62.5 g/ha of the compounds designated as **I** and **J** caused 95 and 98% damage to the plant, respectively. Similar amounts of compound **A** resulted in 100% damage to Sinapis alba, whereas the same amount of the corresponding chloro-substituted prior art compound 5.4 only resulted in 90% damage.

Additionally, the data provided in Declaration 2 illustrate the impact which a structural modification in a position other than R^1 of formula (I) has on the potency of the compound. For example, Tables 1 and 13 set forth data obtained using compounds **A.2** and **M** which differ structurally solely in the nature of R^2:



No.	R^2
A.2	SCH_3
M	Cl

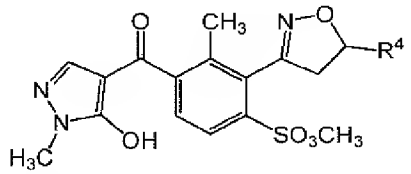
Inter alia the following results were obtained when the compounds were applied at a rate of 250 g/ha. For convenience, the respective data are compiled in the following Table 1E.

Table 1E (*the data are set forth in Tables 1 and 13, on pages 2 and 8, of Declaration 2*) Comparison of the efficacy (*plant damage in percent*) of compounds **A.2** and **M** in accordance with application Ser. No. 09/091,300

Compound	**A.2**	**M**
Chenopodium album	100	100
Polygonum persicaria	98	100
Solanum nigrum	95	98

The data illustrate that the structural modification in the position of R^2 of the compounds (I) does not have a significant impact on the potency of the herbicidal effect.

Tables 8 and 9 of Declaration 2 provide results pertaining to compounds **H** and **I** which are illustrative of the impact on the potency of the herbicidal effect of a change in the position of R^4.



No.	R^4
H	H
I	CH_3

Inter alia the following results were obtained when the compounds were applied at a rate of 125 or 62.5 g/ha. For convenience, the respective data are compiled in the following Table 1F.

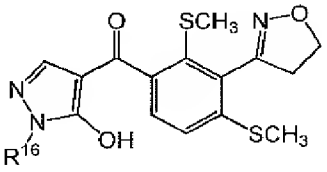
Table 1F (*the data are set forth in Tables 1 and 13, on pages 2 and 8, of Declaration 2*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of compounds **H** and **I** in accordance with application Ser. No. 09/091,300

Application Rate	125 g/ha		62.5 g/ha	
Compound	**H**	**I**	**H**	**I**
Chenopodium album	100	100	100	100
Polygonum persicaria	98	100	98	100
Setaria viridis	98	95	98	90

Although compound **I** which carries a methyl group in the position of R^4 is notably less effective against Setaria viridis at the lower application rate, the data illustrate that the structural modification in the position of R^4 of the compounds (I) generally does not have a significant impact on the potency of the herbicidal effect.

The impact of a modification in the position of R^{16} is, for example illustrated by data in Tables 3 and 4, Tables 13 and 14, and Tables 16 and 17, of Declaration which set forth test results obtained with compounds **C** and **D**, **M** and **N**, and **P** and **Q**, respectively. The pertinent data are compiled for convenience in the following Tables 1G to 1I.

Compounds **C** and **D** which are representative of the compounds (I) as disclosed and currently claimed in application Ser. No. 09/091,300 have the following structure:

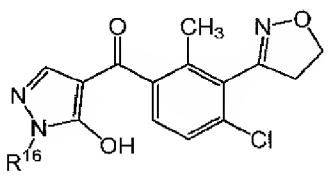


No.	R^{16}
C	CH_3
D	CH_2CH_3

Table 1G (*the data are set forth in Tables 3 and 4, on pages 3 and 4, of Declaration 2*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of compounds **C** and **D** in accordance with application Ser. No. 09/091,300

Application Rate	500 g/ha		250 g/ha	
Compound	**C**	**D**	**C**	**D**
Chenopodium album	98	98	98	98
Ipomoea spp.	100	100	95	95
Setaria faberi	95	95	95	95
Setaria viridis	100	100	100	100

Compounds **M** and **N** which are representative of the compounds (I) as disclosed and currently claimed in application Ser. No. 09/091,300 have the following structure:

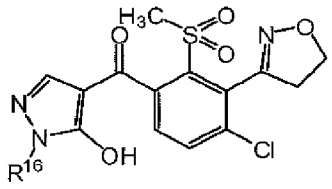


No.	R^{16}
M	CH_3
N	CH_2CH_3

Table 1H (*the data are set forth in Tables 13 and 14, on pages 8 and 9, of Declaration 2*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of compounds **M** and **N** in accordance with application Ser. No. 09/091,300

Application Rate	500 g/ha		250 g/ha	
Compound	**M**	**N**	**M**	**N**
Chenopodium album	100	100	100	100
Polygonum persicaria	100	100	100	100
Solanum nigrum	98	100	98	98

Compounds **P** and **Q** which are representative of the compounds (I) as disclosed and currently claimed in application Ser. No. 09/091,300 have the following structure:

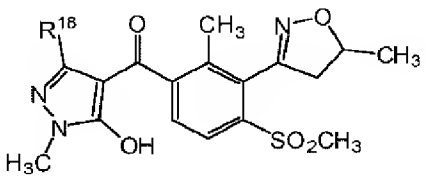


No.	R^{16}
P	CH_3
Q	CH_2CH_3

Table 1I (*the data are set forth in Tables 16 and 17, on page 10, of Declaration 2*) Comparison of the efficacy (*plant damage in percent, side-by-side test*) of compounds **P** and **Q** in accordance with application Ser. No. 09/091,300

Application Rate	250 g/ha		125 g/ha	
Compound	**P**	**Q**	**P**	**Q**
Chenopodium album	100	100	100	100
Polygonum persicaria	100	95	98	95

The test results reflected in Tables 9 and 11 concern compounds **I** and **K** and illustrate the effect on the potency of the compounds when the group in position R^{18} is modified. For convenience, the respective data are reproduced in the following Table 1K.



No.	R^{18}
I	H
K	CH_3

Table 1K (*the data are set forth in Tables 16 and 17, on page 10, of Declaration 2*) Comparison of the efficacy (*plant damage in percent*) of compounds **P** and **Q** in accordance with application Ser. No. 09/091,300

Application Rate	125 g/ha		62.5 g/ha	
Compound	**I**	**K**	**I**	**K**
Chenopodium album	100	100	100	100
Polygonum persicaria	100	100	100	100
Setaria viridis	95	90	90	90

The data which were provided with Declaration 2, thus, provide insights into the particular properties of the compounds disclosed and claimed in application Serial No. 09/091,300 which go beyond what can be deduced on the basis of the comparison of the structurally closes species which is illustrated in Declaration 1. Even the investigations which involved compounds which are not within the scope of current Claim 28 and which are not disclosed by ***von Deyn et al.*** provide valuable information as the results of these investigations further illustrate the trends which are apparent in the herbicidal properties of the compounds. Therefore, I am of the opinion that these data and results should be accorded the same weight as is being given the data and results provided in Declaration 1.

I noticed that the Office action questioned whether the improved herbicidal activity which was shown by the results reported in Declarations 1 and 2 had practical value. In my opinion, the data and results illustrate several advantages which, together, corroborate the practical value of the improved properties of the compounds disclosed and claimed in application Serial No. 09/091,300:

- The data in the foregoing Tables 1B and 1C, for example, show that the compounds in accordance with the present application generally provide a better control of the unwanted plants even if applied at an application rate which is only half of that used for in the application of the prior art compounds. Accordingly, less chemicals are needed and yet, a better result is achieved. Especially the superior control of Amaranth which is achieved by the compounds disclosed and claimed in application Serial No. 09/091,300, as compared to the compounds of ***von Deyn et al.***, is highly relevant since an increasing number of Amaranth species, such as Palmer Ameranth, are tolerant against the herbicide glyphosate (Roundup®) and other key herbicides which are commonly employed, e.g., in corn in the US. The acreage which is infested by such herbicide tolerant Amaranth species continues to grow, thus posing a significant threat to the US agriculture.
- The data in the foregoing Table 1C further show that the compounds in accordance with the present application not only provide a better control of the unwanted plants at half the application rate, as compared to the structurally closest prior art compound, but also are fully tolerated by the crop plant Zea mays at that application rate. Additionally, the broader spectrum of activity, i.e., the control of both grasses and broad-leafed weeds, together with high selectivity to corn, reduces or even eliminates the need to employ the compound in combination with other herbicides or with safeners compared to the prior art compounds and the market standards, and thus further eases the burden on the environment.

I also noticed that the Office action questioned the statistical significance of the data which were provided in my Declarations and criticized that the unexpected results cannot be determined without, e.g., the indication of standard deviations. In my opinion, data as provided in my Declarations allow a determination of the unexpected results although standard deviations and like statistical values were not determined.

Each of the tests was conducted by sowing a multitude of seeds in one pot. Depending on the plant species, the number of seeds varies from about 10 to about 30 seeds per pot. The potted seeds were then grown to the desired growth stage, which is standardizcd for each of the plant species. The herbicide was applied post-emergence to the pot, that is, was applied to from about 10 to about 30 plants, depending on the plant species, with at least one pot remaining untreated to provide a control group. After the application of the herbicide, the treated and untreated pots were kept for 21 days under standardized conditions in the

greenhouse and the damage on the plants which resulted from the treatment with the herbicide was evaluated visually in comparison to the untreated control. Therefore the results set forth in my Declarations are, in each case, ratings which are averaged over many plants. As the control is kept under the same conditions as the treated plants, the error in these visual assessments, albeit not quantified, generally is small.

The rating of the plant damage generally takes into account how many plants survived the treatment as compared to the control collective, as well as factors such as visible damage, i.e., necrosis of the plant tissue, stunting, and the like. The distinct differences between ratings of 100%, 95%, 90% and 80% damage are illustrated by the following photographs of tests conducted with Abutilon theoprasti, Avena sativa, and Echinochloa crus-galli:

Abutilon theoprasti:

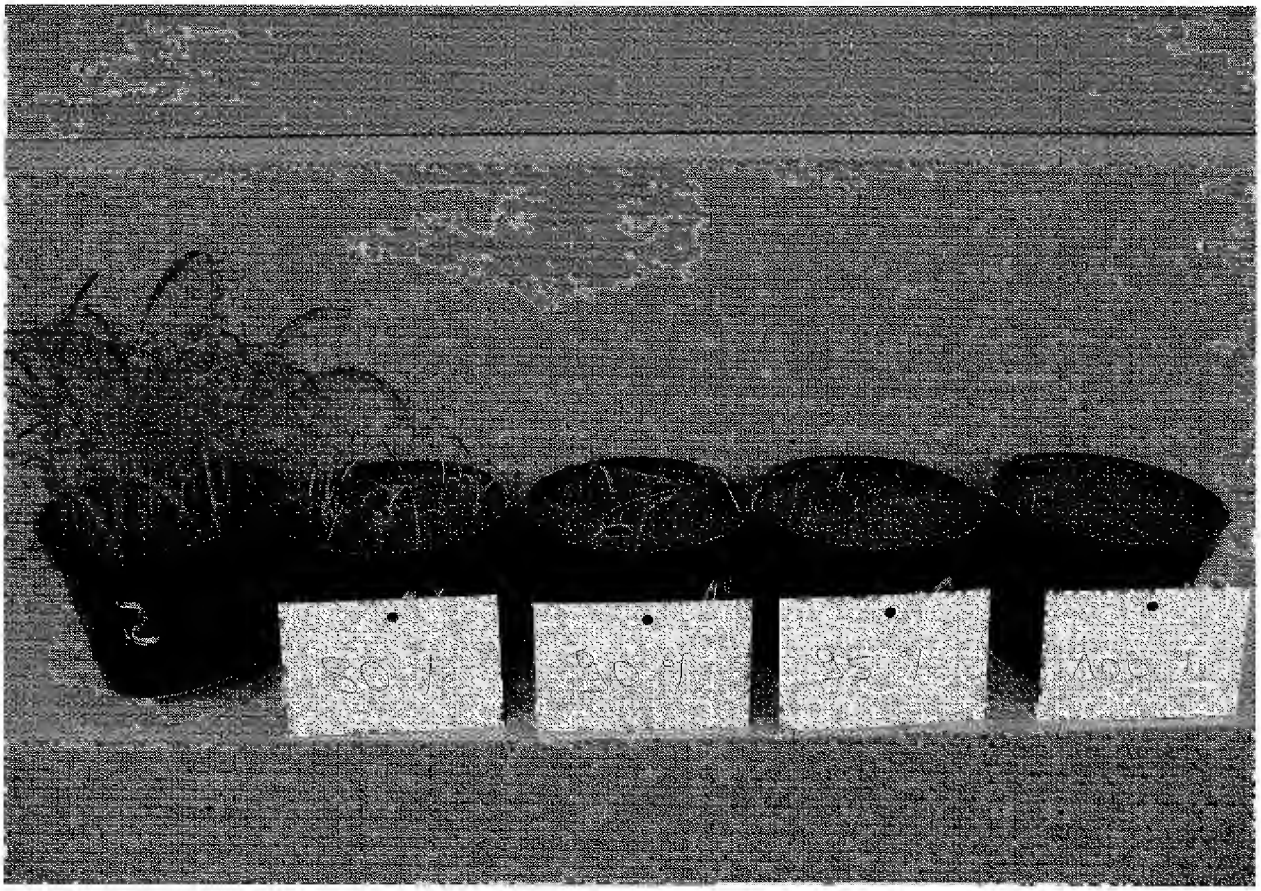
The unmarked pot represents the control experiment, i.e., the untreated plants. It can be seen when the pot marked as 80% is compared with the pot marked as 90% that the number of plants which survived the treatment does not differ significantly. However, the surviving plants in the pot marked as 90% showed significantly more necrosis, and more stunting, than

those of the surviving plants in the pot marked as 80%. When comparing the pots marked 90% and 95%, respectively, it is immediately apparent that the number of surviving plants is further reduced and the growth is stunted more severely in the plants of the pot marked with 95% than is the case in the pot marked with 90%. In the pot marked with 100%, no plants survived, i.e., no green plant tissue evident.

Avena sativa:

Again, the pot furthest left is the control collective. Similar to the previous photograph it is evident when the 80% grade and the 90% grade are compared that the number of plants which survived the treatment is lower at 90% damage than is the case at 80% damage, and the plants graded as 90% damage are more stunted than those graded as 80% damage. Compared to the 90% damage, the plants graded as showing 95% damage exhibit more necrosis and stunting than the plants graded as 90% damaged. Also, the number of plants which survived the treatment in the experiment graded as 95% damage was distinctly lower than that in the experiment graded as 90% damage. In the experiment graded as 100% control, no green plant tissue was evident.

Echinochloa crus-galli:



The differences in the effects which were shown in the foregoing photographs are equally apparent from this photograph. The number of plants which survived the treatment decreases while the stunting and necrosis which is visible on the surviving plants increases as the damage assessment increases, and no green plant tissue is visible when the damage is assessed as 100%.

The foregoing photographs illustrate that a damage which is assessed as 90% differs as distinctly from a damage assessed as 80% as it differs from the damage which is assessed as 95%. Similar distinct differences are evident between other assessed damage values. The damage assessment is normally made under my supervision. Although the damage assessment is done visually and, thus, is subjective it has been my experience that different personnel when assessing the same test arrive at the same damage assessment.

Therefore, it is my opinion that the data and results which are provided in my previous Declarations allow one having ordinary skill in the herbicidal art to assess the difference in the effectivity of the compounds involved in the respective investigations, and to evaluate the surprising and advantageous properties of the compounds disclosed and claimed in application Serial No. 09/091,300 as compared to the properties of the structurally closest prior art compounds.

I, Matthias C. Witschel, further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Date: 19.12.2011

(Matthias C. Witschel)

Encl.: US 4,405,357 with markings